# Prevention and post-exposure management of occupational exposure to Ebola virus

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**There have been significant advances in the prevention and management of Ebola virus disease (EVD) caused by Zaire Ebola virus (ZEBOV), including the development of two effective vaccines, rVSV-ZEBOV and Ad26.ZEBOV/MVA-BN-Filo. In addition, ZEBOV monoclonal antibodies have become first-line therapy for EVD. However, the 2022–23 outbreak of Sudan Ebola virus (SUDV) in Uganda has highlighted the gap in current therapies and vaccines, whose efficacy is uncertain against non-ZEBOV species. Health-care and laboratory staff working in EVD treatment centres or Ebola virus diagnostic and research laboratories face unique risks relating to potential occupational exposure to Ebola viruses. Given the substantial morbidity and mortality associated with EVD, facilities should have strategies in place to manage occupational exposures, including consideration of post-exposure therapies. In this Review, we discuss currently available evidence for prevention and post-exposure prophylaxis of EVD, including therapies currently under evaluation for SUDV.**

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## Background

Ebola virus is a negative-sense, single-stranded RNA virus and member of the Filoviridae family. There are four species in the genus *Ebolavirus* currently known to cause Ebola virus disease (EVD)—namely, Zaire Ebola virus (ZEBOV), Sudan Ebola virus (SUDV), Bundibugyo Ebola virus (BDBV), and Taï Forest Ebola virus (TAFV). They are all considered regionally epizootic in central, western, and eastern African countries.[1] The two remaining species of the genus *Ebolavirus*, Reston Ebola virus and Bombali Ebola virus, are not known to cause human disease.

Since the first reported outbreak of EVD in the Democratic Republic of the Congo (DRC) in 1976,[2] more than 20 EVD outbreaks have emerged in sub-Saharan African countries across west Africa, central Africa, and east Africa.[3] The largest of these occurred between 2014 and 2016 in west Africa, with over 28 000 EVD cases and more than 11 000 deaths from ZEBOV infection reported.[4] The most recent outbreak—from September, 2022, to January, 2023—involved the re-emergence of SUDV in Uganda, resulting in 164 cases and 77 deaths (confirmed and probable cases).[5] The estimated case fatality rate (CFR) of untreated EVD is greater than 50% based on clinical outcomes reported for more than 32 000 individuals with EVD in sub-Saharan Africa.[6,7] The high CFR of EVD has been observed across *Ebolavirus* species, with a recent meta-analysis reporting CFRs greater than 50% for ZEBOV, SUDV, and BDBV.[6] Only a single human case of TAFV infection has been reported to date, with a non-fatal outcome.[8] Fewer than 20 EVD cases have been managed outside of sub-Saharan Africa; they were related to infection in travellers or health-care workers returning from EVD outbreak regions.[3]

The incubation period of EVD ranges from 2 to 21 days (typically 6–10 days), with common disease manifestations including fever, vomiting, diarrhoea, and rash; bleeding manifestations occur in less than half of patients.[1] Person-to-person transmission occurs primarily through direct contact with body fluid from people with EVD. The highest risk of person-to-person transmission, therefore, occurs in late stages of severe disease, when vomiting, diarrhoea, and bleeding diathesis are more likely to occur.[9] Zoonotic transmission to humans is likely a result of direct contact with wild animals—eg, through hunting or butchering, or through contact with fruit bats, the putative viral reservoir host.[10]

Ebola viruses gain entry to host cells through an endocytic pathway, mediated by the viral transmembrane glycoprotein.[11,12] Components of the viral glycoprotein have been identified as major antigenic targets for neutralising antibodies in survivors of EVD,[13] thereby leading to the development of vaccines and monoclonal

### Key messages

- Outbreaks of Ebola virus disease (EVD) have caused significant morbidity and mortality in sub-Saharan African countries, most recently observed during the Sudan Ebola virus (SUDV) outbreak in Uganda
- Health-care and laboratory workers managing people with EVD or handling infectious samples are at increased risk of Ebola virus acquisition through occupational exposure
- Effective vaccines are available for pre-exposure prevention of EVD caused by the Zaire Ebola virus (ZEBOV), but cross-protection against EVD caused by non-ZEBOV species is not always known; SUDV monovalent and multivalent Ebola virus vaccines are currently being investigated
- Following occupational exposure, a post-exposure risk assessment should be done to determine further management, including consideration of post-exposure prophylaxis
- Monoclonal antibody therapies are now first-line treatments for EVD but do not have activity against non-ZEBOV species; antivirals and monoclonal antibody therapies are currently being evaluated for activity against SUDV

antibodies (mAbs) targeting the ZEBOV glycoprotein. However, the glycoprotein structure is not conserved across species, with 30% divergence at an amino acid level between glycoproteins from ZEBOV, SUDV, and BDBV.[14] Disease pathogenesis in EVD is thought to be related to direct viral infection of, and resulting cytopathic effect on, multiple cell types, suggesting broad tissue tropism, including antigen-presenting cells, fibroblasts, hepatocytes, and endothelial and epithelial cells.[15] In addition, infection leads to a systemic inflammatory response syndrome, resulting in downregulation of innate immune responses mediated by interferon, as well as pronounced cytokine release that contributes to multiorgan failure and coagulopathy.[15]

In countries with low risk of EVD occurrence, cases of EVD are usually managed in dedicated treatment facilities with access to biosafety level 4 (BSL-4) high-containment laboratory facilities. BSL-4 facilities ensure maximum protection to both staff and the community when managing such patients or handling specimens with potentially infectious material. In contrast, there is limited access to BSL-4 facilities in remote and resource-limited settings where EVD outbreaks have emerged. Mobile field laboratories with biosafety level 3 (BSL-3)-like conditions are instead deployed for rapid establishment of testing facilities at the epicentre of EVD outbreaks.[16,17] Appropriate training and adherence to biosafety practices remain paramount for prevention of hazardous occupational exposure. In particular, mobile field laboratories rely on highly trained staff to safely inactivate and test samples outside of a BSL-4 facility using personal protective equipment (PPE) in negatively pressurised glovebox systems.[16,17] Rigorous training is also required for laboratory workers in BSL-4 facilities outside outbreak regions, with increased laboratory handling of Ebola viruses occurring in the setting of upscaled vaccine and therapeutics research, with EVD being listed a priority disease by both the Coalition for Epidemic Preparedness Innovations and WHO.[18,19]

Occupational exposure to Ebola viruses remains a significant risk, with documented cases of high-risk exposures in EVD treatment centres[20–23] and in BSL-4 research laboratories.[24] Risk is greatest for individuals working in the field during EVD outbreaks. During the recent SUDV outbreak in Uganda, 19 (13·4%) of 142 EVD cases and seven deaths occurred in health-care workers.[5] Health-care workers were also 21–32 times more likely to be infected with ZEBOV during the 2014–16 west African epidemic compared to the general adult population.[25] Transmission in the health-care setting can occur from direct inoculation—eg, needlestick injury—or through a breach in PPE while managing a patient with EVD. In addition, exposure to patients with unrecognised EVD has been associated with increased risk of health-care Ebola virus acquisition,[26] which can occur if EVD is not initially suspected and inadequate PPE is used during the screening or triage process. Self-contamination during PPE doffing also poses a risk for health care-acquired EVD.[27]

In the laboratory, additional risks can occur through handling of specimens with high viral concentrations.[24] These risks are highest in the outbreak setting, where risk mitigation with biosafety cabinets and BSL-4 laboratory facilities are unavailable, placing greater dependence on stringent PPE use in mobile field laboratories. Samples received before recognition of EVD risk can also lead to hazardous exposure if they are inadvertently processed and tested outside of appropriate infection prevention precautions. The number of laboratory-acquired Ebola virus infections that have occurred during EVD outbreaks in the field is unknown; however, 48 (6·7%) of 718 EVD cases in health workers in the 2014–16 west African epidemic occurred among laboratory workers.[25] In areas of low EVD occurrence outside sub-Saharan Africa, several laboratory incidents have been described as leading to high-risk exposure to Ebola viruses,[24,28] with three cases of confirmed laboratory-acquired EVD reported.[3,29,30] The most recently documented case of laboratory-acquired infection with ZEBOV was in 2004, with a fatal outcome; it was related to a needlestick injury in a scientist working in a BSL-4 research laboratory in Russia.[30] The researcher died 14 days after the incident.

The availability of vaccines and mAbs targeted to ZEBOV offers opportunities to improve safety for clinical and laboratory staff managing patients with suspected and confirmed EVD, or handling Ebola virus-positive samples. However, access to these therapies is limited. Moreover, it is not always known whether current EVD vaccines and therapies provide cross-protection against other *Ebolavirus* species, including SUDV, which recently circulated in Uganda.[31–33] Staff working in EVD treatment centres and BSL-4 laboratories with potential exposure to Ebola virus should receive rigorous and regular training in infection prevention and biosafety practices. In addition, there should be established pathways for managing accidental occupational exposure to Ebola virus, including procedures for post-exposure prophylaxis (PEP) and follow-up monitoring. Here, we review currently available evidence for pre-exposure vaccination and PEP for EVD.

## Pre-exposure vaccination

There are currently two Ebola vaccines listed by WHO for use in protection against ZEBOV: a single-dose, live-attenuated vaccine, rVSV-ZEBOV (ERVEBO; Merck, Rahway, NJ, USA), and a two-dose, prime–boost vaccine, Ad26.ZEBOV (Zabdeno) and MVA-BN-Filo (Mvabea; both from Janssen Pharmaceuticals, Beerse, Belgium). rVSV-ZEBOV was approved by the US Food and Drug Administration (FDA) in 2019 as a single-dose vaccine for prevention of ZEBOV.[34] It is the only vaccine currently approved by the FDA for EVD. The Ad26.ZEBOV and MVA-BN-Filo vaccine regimen was granted marketing

authorisation under exceptional circumstances by the European Medicines Agency in 2020.[35]

### rVSV-ZEBOV

rVSV-ZEBOV consists of live-attenuated, recombinant vesicular stomatitis virus (VSV) with the gene encoding the glycoprotein of VSV replaced by the gene encoding the glycoprotein of ZEBOV.[36] It does not induce protective immunity against *Ebolavirus* species other than ZEBOV.[31] It is manufactured as a live vaccine in Vero cells, and as a live vaccine, it has an unclear safety profile and efficacy in immunocompromised individuals. Use of rice-derived recombinant human serum albumin in the vaccine also precludes its use in people with severe allergy to rice protein.

Vaccine effectiveness of rVSV-ZEBOV was reported to be 100% (95% CI 68·9–100·0) in a phase 3, open-label, cluster-randomised trial in Guinea and Sierra Leone, conducted during the 2014–16 ZEBOV outbreak.[37] Clusters were randomised to either immediate vaccination or delayed vaccination (21 days later), with eligible participants including contacts, or contacts of contacts, of a confirmed case. No laboratory-confirmed cases of EVD occurred 10 days or more following vaccination in over 5800 individuals who received immediate vaccination, including 194 children. In contrast, there were 16 confirmed EVD cases in the 2041 individuals who were part of the delayed vaccination group in the randomised part of the trial. At least one adverse event was reported by 3149 (53·9%) of 5837 vaccinees, with headache (1832 [25·4%] of 7211 total recorded adverse events), fatigue (1361 [18·9%]), and muscle pain (942 [13·1%]) being most common. Two serious adverse events related to the vaccine were reported—one febrile reaction and one episode of anaphylaxis (one [0·02%] in 5837 vaccine doses administered). A sub-study of front-line workers (n=1172) demonstrated that a single dose of rVSV-ZEBOV induced an IgG response to ZEBOV glycoprotein in 86% of participants at 28 days post-vaccination, and a neutralising antibody response against ZEBOV glycoprotein was detected in 83% of individuals.[38] Similar responses were observed in a cohort of vaccinated individuals (n=608) in DRC, conducted during the 2018–20 outbreak.[39] 21 days after vaccination with rVSV-ZEBOV, 478 (87·2%) of 548 returning participants had an anti-ZEBOV glycoprotein antibody response, and 95·6% (415 of 434) had persistence of anti-ZEBOV glycoprotein antibodies at 6 months. rVSV-ZEBOV was subsequently administered to 345 000 individuals during the 2018–20 Ebola virus outbreak as part of a ring vaccination strategy.[40]

The US Advisory Committee on Immunization Practices made recommendations in 2020 for pre-exposure vaccination with rVSV-ZEBOV to be given to adults aged 18 years and older at highest risk of potential occupational exposure to ZEBOV.[41] This includes laboratory workers in BSL-4 facilities and health-care workers at federally designated EVD treatment centres in the USA.[41] Duration of protection conferred by the vaccine is currently unknown. Total anti-ZEBOV glycoprotein antibodies have been shown to persist 1–2 years after vaccination in healthy individuals, although neutralising antibodies decreased after 6 months.[42] However, it is unclear what impact the decline in neutralising antibodies has on protection against disease.[42] In non-human primates, lower protection against ZEBOV challenge was observed at 3 months and 1 year post-vaccination than at 42 days: two (33·3%) of six animals and three (42·8%) of seven animals survived following ZEBOV challenge at 3 months and 1 year, respectively, compared to 100% protection observed following ZEBOV challenge at 42 days post-vaccination.[43] Yet, neutralising antibody levels before ZEBOV challenge did not predict survival.[43]

Given the uncertainty in duration of clinical protection in humans following vaccination, the US Centers for Disease Control and Prevention (CDC) has endorsed booster-dose administration of rVSV-ZEBOV for at-risk adults in whom vaccination occurred at least 6 months before through an expanded access programme.[44] Eligibility is restricted to those at highest risk, including individuals responding to an outbreak of EVD (eg, deployed to an outbreak area or working in a US designated EVD treatment centre), and laboratory personnel in BSL-4 laboratories who might handle Ebola virus-infected materials.[44] In a recently published randomised trial of vaccines for ZEBOV, the immune response to rVSV-ZEBOV was evaluated among participants administered either a booster dose at 56 days or placebo. Administration of a booster dose resulted in only a transient increase in antibody concentrations, with comparable levels among both groups at 12 months.[45] The effect of booster doses given at later intervals is being evaluated in additional trials (NCT02788227 and NCT05959421). Recommendations for booster vaccination of high-risk health-care or laboratory workers have not yet been made by other international agencies, including for health-care workers who have previously been vaccinated for work in EVD outbreak areas.

### Ad26.ZEBOV and MVA-BN-Filo

Ad26.ZEBOV is a monovalent, adenovirus 26 (Ad26)-vectored vaccine that encodes the ZEBOV glycoprotein.[46] Ad26.ZEBOV is given as the first-dose priming vaccination and is specific to ZEBOV. The second component, MVA-BN-Filo, is a multivalent modified vaccinia Ankara-vectored vaccine that expresses glycoproteins from ZEBOV, SUDV, TAFV, and Marburg virus.[46] MVA-BN-Filo is administered 8 weeks after Ad26.ZEBOV. Both vaccines are replication defective in human-derived cell lines. This combination vaccine has been demonstrated to be safe and immunogenic for ZEBOV,[46–49] including in people living with HIV.[50] Although there are

currently no clinical data on cross-protection against non-ZEBOV species in humans, the Ad26.ZEBOV and MVA-BN-Filo prime–boost vaccine strategy has been shown to elicit SUDV neutralising antibodies and to protect against lethal challenge with SUDV in non-human primates (n=5).[51] The Ad26.ZEBOV priming dose has been shown to elicit an anti-ZEBOV glycoprotein response in more than 90% of individuals before the second dose;[49] however, it has not been evaluated as part of a ring-vaccination strategy in an outbreak response, where immediate protection is necessary. The durability of the antibody response at 1 year for participants receiving the two vaccines 8 weeks apart was 100% for anti-ZEBOV glycoprotein antibodies and 52% for neutralising antibodies.[49] A phase 3 clinical trial to evaluate the effectiveness of the Ad26.ZEBOV and MVA-BN-Filo vaccine regimen commenced in 2019 during the ZEBOV outbreak in eastern DRC.[52] More than 20 000 participants, including pregnant women and children, received the vaccine; however, resolution of the outbreak in mid-2020 precluded assessment of vaccine effectiveness.[52] Results on vaccine safety and immunogenicity have not yet been reported.

### Vaccines in development

Several monovalent vaccines, each targeting the ZEBOV glycoprotein, have been evaluated in phase 1 and 2 clinical trials but are not licensed for use in the USA. These include ChAd3-EBO-Z, a replication-defective chimpanzee adenovirus 3 (ChAd3)-vectored vaccine encoding the ZEBOV glycoprotein;[53,54] Ad5-EBOV, a recombinant adenovirus 5 (Ad5)-vectored vaccine expressing the ZEBOV glycoprotein that is licensed for emergency use in China;[55] GamEvac-Combi, a two-dose prime–boost vaccine regimen that uses live-attenuated recombinant VZV as the first dose and a recombinant replication-defective Ad5-vectored vaccine expressing ZEBOV glycoprotein as the second dose (licensed for emergency use in Russia);[56] INO-4201, an intradermal DNA vaccine;[57] and a recombinant ZEBOV glycoprotein nanoparticle-based vaccine.[58]

Given the recent outbreak of SUDV in Uganda, a review was conducted by the WHO Vaccine Prioritization Working Group of vaccines with potential activity against SUDV.[59] Three candidate vaccines were endorsed for inclusion in a planned randomised trial of ring vaccination in Uganda: VSV-SUDV, ChAd3-SUDV, and biEBOV. VSV-SUDV is a single-dose, transgenic, live-attenuated vaccine encoding SUDV glycoprotein that has demonstrated protection against clinical disease in cynomolgus macaques (n=6) following challenge with SUDV.[60] ChAd3-SUDV is a monovalent, ChAd3-vectored vaccine encoding the SUDV glycoprotein. The ChAd3 vaccine platform has been evaluated previously as a monovalent vaccine for ZEBOV[53,54] and as a bivalent vaccine targeting ZEBOV and SUDV glycoproteins; it has been shown to be safe and well tolerated.[61] biEBOV is a bivalent, replication-deficient, simian adenovirus-vectored (ChAdOx1) vaccine encoding both ZEBOV and SUDV glycoproteins.[59] Results of a phase 1 trial for ChAd3-SUDV vaccine have recently been reported.[62] Published data on additional, recently completed phase 1 studies for both ChAd3-SUDV and biEBOV vaccines are awaited (NCT04723602, NCT05079750, and NCT05301504).

In addition to these three candidate vaccines, several multivalent vaccines with activity against SUDV have been evaluated in phase 1 clinical trials.[61,63] Ad26.Filo is a multivalent, recombinant, Ad26-vectored vaccine comprising Ad26.ZEBOV, Ad26.SUDV, and Ad26.MARV, encoding ZEBOV, SUDV, and Marburg virus glycoproteins, respectively. Similar to Ad26.ZEBOV, Ad26.Filo is given as part of a two-dose schedule with MVA-BN-Filo. The Ad26.Filo and MVA-BN-Filo vaccine regimen was well tolerated and demonstrated robust neutralising antibody responses against ZEBOV (86–100%), but variable responses against SUDV (36–100%) and Marburg virus (0–57%), depending on the time interval between first and second doses.[63] The bivalent vaccine, cAd3-EBO, uses the ChAd3 vaccine platform and encodes both ZEBOV and SUDV glycoproteins.[61] It was evaluated in a phase 1 clinical trial in 20 participants and demonstrated 90–100% antibody response to ZEBOV glycoprotein and 70–80% to SUDV glycoprotein 4 weeks after a single dose.[61]

## Post-exposure case management

A rapid risk assessment should be performed following potential occupational exposure to Ebola virus. Factors that should be considered include the mechanism of exposure (eg, needlestick), the potential inoculum size, whether a PPE breach was involved, and the vaccination status, underlying immunosuppression, and other medical comorbidities of the exposed individual. Various risk stratification recommendations have been made for potential occupational exposure to Ebola virus (figure). In 2014, the US CDC issued interim guidance for monitoring and movement of people with potential ZEBOV exposure, stratifying them into high risk, some risk, low (but not zero) risk, and no identifiable risk.[64] In the most recent recommendations issued by the UK Health Security Agency (UKHSA) in 2021, three risk categories were identified for returning workers who were asymptomatic contacts of people with EVD.[65] A more detailed stratification by exposure type, and an algorithm for post-exposure management, including use of PEP, were developed and proposed by Jacobs and colleagues[22] on the basis of a case series in eight health-care workers. PEP was offered to individuals assessed as having at least an intermediate risk of developing EVD (n=4).[22] Individuals who received PEP were hospitalised for 10 days for monitoring, with PCR performed daily on blood samples for the duration of hospitalisation. They were then discharged to the community for a further 21 days of monitoring. The extended monitoring,

| Jacobs et al (2015)[22] | US CDC interim guidance (2014)[64] | UK Health Security Agency[65] |
|---|---|---|
| **Very low risk**<br>Close contact (<1 m) with a patient with EVD without wearing PPE but no direct contact with patient | **Low (but not zero) risk**<br>Having been in a country with widespread Ebola virus transmission within the past 21 days and having had no known exposures<br>or<br>Having brief direct contact (eg, shaking hands), while not wearing appropriate PPE, with a person with EVD while the person was in the early stage of disease<br>or<br>Brief proximity, such as being in the same room for a brief period of time, with a person with EVD while the person was symptomatic | **Category 1**<br>UK aeromedical staff undertaking a controlled patient transfer under extant standard operating procedures<br>or<br>Laboratory staff in a biosafety level 4 laboratory assured to be operating to UK standards<br>or<br>A person who has visited an Ebola-affected area but had no direct contact with patients with EVD (or body fluids) |
| **Low risk**<br>Close contact (<1 m) with a patient with EVD without wearing PPE and direct contact with patient; patient did not have diarrhoea, vomiting, or bleeding | **Some risk**<br>In countries with widespread Ebola virus transmission: direct contact while using appropriate PPE with a person with EVD while the person was symptomatic<br>or<br>Close contact (<1 m for a prolonged period) with a person with EVD while the person was symptomatic while not wearing appropriate PPE | **Category 2**<br>Direct (close) contact with people with EVD or their body fluids (but did not provide direct physical contact as part of clinical care), but trained and wore appropriate PPE with no known breaches |
| **Intermediate risk**<br>Close contact (<1 m) with a patient with EVD without wearing PPE and direct contact with patient; patient had diarrhoea, vomiting, or bleeding<br>or<br>Direct contact with body fluids from a patient with EVD or environment visibly contaminated with body fluids with no contamination of broken skin or mucous membranes<br>or<br>Needlestick injury in an area where patients with EVD are managed; needle was not freshly used and not known to have had contact with a patient with EVD | **High risk**<br>Percutaneous (eg, needlestick) or mucous membrane exposure to blood or body fluids of a person with EVD while the person was symptomatic<br>or<br>Exposure to blood or body fluids of a person with EVD while the person was symptomatic without appropriate PPE<br>or<br>Processing blood or body fluids of a person with EVD while the person was symptomatic without appropriate PPE or standard biosafety precautions<br>or<br>Direct contact with a dead body without appropriate PPE in a country with widespread Ebola virus transmission | **Category 3**<br>Direct contact with a symptomatic case with potential exposure to body fluids (includes vomit, and faeces)<br>or<br>Direct physical contact as part of clinical care, or contact with body fluids, with or without appropriate PPE, including those handling burials, and irrespective of known breaches<br>or<br>Laboratory staff in facilities not assured to be operating to UK standards<br>or<br>Direct exposure of skin or mucous membranes to potentially infectious blood or body fluids, including on clothing and bedding; this includes unprotected handling of clinical or laboratory specimens, mucosal exposure to splashes, and needlestick injury |
| **High risk**<br>Direct contact with body fluids from a patient with EVD or environment visibly contaminated with body fluids with contamination of broken skin or mucous membranes<br>or<br>Needlestick injury in an area where patients with EVD are managed; needle was not freshly used but was known to have had contact with a patient with EVD<br>or<br>Needlestick injury in an area where patients with EVD are managed; needle was freshly used but was not hollow-bore and was known to have had contact with a patient with EVD | | |
| **Maximum risk**<br>Needlestick injury in an area where patients with EVD are managed; needle was freshly used, hollow-bore, and known to have had contact with a patient with EVD | | |

***Figure:*** **Comparison of risk stratification following occupational exposure to patients with EVD or infectious materials**
CDC=Centers for Disease Control and Prevention. EVD=Ebola virus disease. PPE=personal protective equipment.

totalling 28 days, was undertaken to account for potential delayed onset of clinical symptoms following antiviral therapy. Individuals deemed low or very low risk were managed in the community for 21 days and did not receive PEP. Serology was not performed as part of the algorithm owing to lack of availability of serological assays. Monitoring for 21 days post-exposure is in keeping with US CDC and UKHSA recommendations.[64,65] However, modelling data suggest the incubation period of ZEBOV could be longer than 21 days in some individuals (predicted 4·1%), indicating that it would be appropriate to extend monitoring to 25 days to cover the maximum predicted incubation period.[66] These modelling data are limited by incomplete information regarding date of exposure, with several estimates made of likely time of acquisition.[66]

Baseline serology has been recommended for laboratory workers handling specimens from individuals with confirmed EVD.[67] Repeat serology for ZEBOV at the time of occupational exposure (repeat baseline), followed by convalescent testing (4–6 weeks later) should be considered to assess for subclinical infection. The exact

frequency of asymptomatic ZEBOV infection is unknown, with serostudies suggesting that it could range from as low as 2·6%,[68] up to 30%.[69] In a study evaluating ZEBOV seropositivity in patients with clinically suspected EVD who tested negative for ZEBOV by PCR, 11 (2·3%) of 488 samples were found to be seropositive (reactive to two ZEBOV antigens), compared to 0·4% in the control group.[70] The authors concluded that PCR alone might miss a proportion of pauci-symptomatic ZEBOV infection. Table 1 summarises published cases of post-exposure management following occupational exposure to ZEBOV.

## PEP

Evidence to guide choice of PEP is limited and is extrapolated from clinical and preclinical studies for

| | Günther et al (2011)[24] | Lai et al (2015)[20] | Cnops et al (2015)[21] | Jacobs et al (2015)[22] | Davis et al (2019)[71] | Jaspard et al (2021)[23] |
|---|---|---|---|---|---|---|
| Date of exposure | March, 2009 | September, 2014 | December, 2014 | January–March, 2015 | October, 2015 | July, 2019–January, 2020 |
| Location of care | Hamburg, Germany | USA (medically evacuated from Sierra Leone) | Belgium (medically evacuated from Liberia) | UK (medically evacuated from Sierra Leone) | UK (previously worked in Sierra Leone) | Democratic Republic of the Congo |
| Exposure | Needlestick injury in a biosafety level 4 laboratory during a mouse experiment; the syringe contained ZEBOV from ultracentrifuged concentrated culture supernatant (traces in syringe contained $1{\cdot}4 \times 10^8$ copies per mL of ZEBOV) | Physician needlestick injury while working in an EVD treatment centre (18G hollow-bore needle that had vented a plastic intravenous bottle)—the needle punctured two layers of gloves and caused bleeding of the thumb; the outer glove had been used in direct contact with severely ill patients with EVD | Needlestick injury (unused needle) punctured through two gloves that had been used in contact with the skin of a patient with confirmed EVD | Eight health-care workers: four low risk (one with eye splash when removing PPE after chlorine was sprayed, one with a tear in PPE after a fall leading to a bleeding skin graze in an EVD treatment centre, one who assessed a patient with EVD before a confirmed diagnosis without PPE with skin contact only, and one who obtained a nasopharyngeal swab from a patient with early EVD before a confirmed diagnosis without mucosal protection but no body fluid exposure), two intermediate risk (both with penetrating needlestick injury through contaminated gloves; in one case the needle was unused and in the other it was unclear if the needle had been used), and two maximum risk (hollow-bore needlestick injury with a needle recently used in a patient with EVD) | 65 individuals (health-care workers and household contacts of a nurse with confirmed EVD with late reactivation); 45 were assessed as high risk (category 3)—ie, not wearing full PPE and had direct contact with body fluids from a patient with EVD | 4 health-care workers included in this study of 23 individuals who received either ansuvimab (n=21) or REGN-E3B (n=2) mAb targeting ZEBOV as PEP; classified as either high risk (direct contact with skin barrier breach with a confirmed EVD patient) or intermediate risk (direct contact without skin barrier breach with an EVD patient) |
| PCR testing frequency | RT-PCR plasma and peripheral blood mononuclear cells daily | Daily while inpatient | Daily until day 9 | Intermediate risk or higher: RT-PCR daily for 10 days while inpatient | Only if temperature ≥37·5°C, on days 14 and 28 following vaccination | RT-PCR daily for 14 days |
| Serology | Not performed | Not performed | Not performed | Not available | Yes (for vaccination recipients), on days 14 and 28, then 3 months, 6 months, 9 months, and 12 months after vaccination | Not performed |
| Hospitalised | Yes, 24 h after exposure | Yes, admitted into isolation room (2 days after exposure) | Yes, admitted on arrival to Brussels (2 days after exposure) | Four low-risk cases monitored in the community; intermediate-risk and maximum-risk cases hospitalised for 10 days during treatment period | No | Not discussed |
| Infection prevention in hospital | Single room with anteroom, negative pressure; PPE included gown, gloves, N95 mask, and eye protection; if the patient became RT-PCR positive, had a rise in D-dimer, or developed a fever, they were to be transferred to the biocontainment patient care unit | Full-contact and respiratory PPE, including a powered air-purifying respirator | Not discussed | Enhanced PPE with fluid-repellent gown, surgical cap, filtering face piece 3 mask, disposable full-face visor, and double gloves only during phlebotomy; otherwise, only basic contact precautions (disposable apron, single gloves, and hand hygiene) used for hospital care | Not applicable | Not discussed |
| Discharge time | After 21 days of isolation | When RT-PCR result was negative on day 9 (day 7 of admission), patient was discharged to home isolation (for 21 days) | Not discussed | 21 days of community monitoring (as per UK public health recommendations[65]) for low-risk cases; for cases at intermediate risk or higher, patients spent 10 days in hospital, followed by 21 days of community monitoring | 21 days of community monitoring | Not discussed |

(Table 1 continues on next page)

| | Günther et al (2011)[24] | Lai et al (2015)[20] | Cnops et al (2015)[21] | Jacobs et al (2015)[22] | Davis et al (2019)[71] | Jaspard et al (2021)[23] |
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| (Continued from previous page) | | | | | | |
| Monitoring | Daily monitoring of body temperature, D-dimer level, full blood examination, biochemistry panel, RT-PCR | Daily full blood examination, biochemistry panel, D-dimer, and RT-PCR while inpatient | Not discussed | Low-risk cases were monitored at home twice daily with temperature recordings for 21 days according to UK public health recommendations;[65] cases at intermediate risk or higher had daily full blood examination and biochemistry panel for 10 days, then discharged with twice daily temperature recordings as per UK policy for 21 days (given risk PEP might delay incubation) and with advice to report illness for up to 42 days after exposure | For high-risk (category 3) exposure, daily temperature screening for 3 weeks in the community; vaccinated individuals had follow-up at days 14, then 1 month, 3 months, 6 months, 9 months, and 12 months after vaccination | Not discussed |
| PEP | rVSV-ZEBOV (not licensed at the time) | rVSV-ZEBOV vaccination (not licensed at the time), given 43 h after needlestick incident and obtained through emergency Investigational New Drug application and institutional review board approval | rVSV-ZEBOV | Intermediate-risk and maximum-risk cases received high-dose favipiravir (loading doses given every 8 h on treatment day 1 [2400 mg, 2400 mg, and 1200 mg], then maintenance dose of 1200 mg twice a day) for 10 days; the two maximum-risk patients also received mAb (one received ZMAb* on day 2 after exposure [50 mg/kg intravenously] and MIL77† on day 5 after exposure [50 mg/kg intravenously], and one received MIL77† on days 2 and 5 after exposure [50 mg/kg per dose intravenously]) | rVSV-ZEBOV vaccine given to 26 high-risk individuals who consented | mAb, either ansuvimab (n=21) or REGN-E3B (n=2); not documented which mAb was received by the four health-care workers |
| Processing of samples | If RT-PCR negative, routine laboratory investigations were to be done by clinical chemistry department without special precautions; if PCR not available in a timely manner, point-of-care diagnostics performed | Not discussed | Not discussed | Not discussed | Not discussed | Not discussed |
| Developed EVD? | No | No | No | No | No | No |
| Other comments | Low positive RT-PCR for ZEBOV glycoprotein gene (expressed in the live vaccine) but negative for L gene (specific for ZEBOV) | Transient positive RT-PCR for vesicular stomatitis virus nucleoprotein gene and ZEBOV glycoprotein gene (both included in the vaccine), but negative for ZEBOV nucleoprotein gene | In-house RT-PCR remained positive 5 days after vaccination (targeting ZEBOV glycoprotein); raises importance of using two PCR targets | .. | .. | .. |

EVD=Ebola virus disease. mAb=monoclonal antibody. PEP=post-exposure prophylaxis. PPE=personal protective equipment. RT-PCR=real-time PCR. ZEBOV=Zaire Ebola virus. *ZMAb is a research-grade combination of a mouse mAb (4G7) and two chimeric human–mouse neutralising mAbs (Public Health Agency of Canada). †MIL77 is a clinical-grade combination of three recombinant afucosylated humanised mAbs (13C6, 2G4, and 4G7; Beijing MabWorks Biotech, Beijing, China).

***Table 1:*** **Summary of published experience of post-exposure management following occupational exposure to ZEBOV**

treatment of EVD. In all instances, informed patient consent should be sought, and treatment should be offered in line with the WHO report on *Ethical Considerations for Use of Unregistered Interventions for Ebola Viral Disease* (the MEURI ethical framework).[72] Facilities should consider having predefined risk-assessment protocols and pathways to access PEP therapies rapidly if needed, both in high-risk settings during EVD outbreaks and in low-risk settings such as BSL-4 diagnostic and research centres, where ready access to vaccine, mAbs, or antivirals might be limited. Currently available EVD therapeutics and therapies advancing into clinical trials are summarised in table 2.

## Post-exposure vaccination and mAbs

Early cases of high-risk occupational exposure were managed by administration of rVSV-ZEBOV vaccine, prior to rVSV-ZEBOV being licensed for use as prevention.[20,21,24,71] In these studies, vaccination was administered within 48 h of exposure and no reported cases of EVD developed. However, rVSV-ZEBOV is only effective for the ZEBOV species. Furthermore, the FDA-approved mAbs ansuvimab (mAb114, Ebanga) and REGN-EB3 (Inmazeb), which are directed against ZEBOV, might be preferred, given their activity is immediate and not dependent on the host immune response.

Ansuvimab is a monoclonal neutralising antibody targeting the receptor-binding domain of the ZEBOV

glycoprotein.[73] REGN-EB3 is an antibody cocktail comprising three mAbs—maftivimab (REGN3479), odesivimab (REGN3471), and atoltivimab (REGN3470)—each targeting different epitopes of the ZEBOV glycoprotein.[77] Ansuvimab and REGN-EB3 are now recommended as first-line therapies for confirmed ZEBOV-related EVD in the WHO therapeutics for EVD clinical management guideline.[98] This recommendation was made following a four-arm, randomised, controlled trial in 681 patients with EVD,[75] wherein both ansuvimab and REGN-EB3 demonstrated significant mortality benefit (35·1% and 33·5% mortality at 28 days, respectively) over the antiviral remdesivir (53·1% mortality) and an alternative antibody cocktail ZMapp (49·7% mortality).

Use of ansuvimab and REGN-EB3 as PEP was also evaluated in a small prospective study in 23 individuals assessed as being at high risk of developing EVD following community or occupational exposure through close contact with a confirmed case.[23] Median time to

| | Mechanism of action and target site | Reported *Ebolavirus* species targeted | Non-human primate studies | Clinical trials | Refs |
|---|---|---|---|---|---|
| **Licensed treatments for EVD by the US FDA** | | | | | |
| Ansuvimab (mAb114) | Glycan cap and core domain of GP1 | ZEBOV | Rhesus macaques (n=3) were protected from lethal ZEBOV challenge when ansuvimab (50 mg/kg) was administered up to 5 days after ZEBOV challenge (100% survival); transient viraemia was observed in all treated animals[73] | Phase 1 clinical trial (n=19) reported mild systemic symptoms (malaise, myalgia, and headache) in 22% of participants;[74] phase 2–3 clinical trial (PALM trial; n=681) reported a mortality benefit at 28 days with ansuvimab (50 mg/kg single dose; 35·1% mortality) compared to remdesivir (53·1%) or ZMapp (49·7%)[75] | 73–76 |
| REGN-EB3 | mAb cocktail comprising three mAbs targeting the ZEBOV glycoprotein: REGN 3479 (targeting the conserved GP2 fusion loop), REGN 3471 (targeting the outer glycan cap), and REGN 3470 (targeting the GP1 head) | ZEBOV | REGN-EB3 administered 5 days post-ZEBOV challenge protected rhesus macaques from lethal disease using 50, 100, or 150 mg/kg single doses (85% survival, n=27); virus load reduction by >$10^6$ fold was observed after therapy[77] | Phase 1 clinical trial (n=24) reported only mild to moderate adverse events (headache most common);[78] phase 2–3 clinical trial (PALM trial; n=681) reported a mortality benefit at 28 days with REGN-EB3 (150 mg/kg single dose; 33·5% mortality) compared to remdesivir (53·1%) or ZMapp (49·7%)[75] | 75–78 |
| **Unlicensed and investigational antiviral agents for EVD** | | | | | |
| Remdesivir | Nucleotide analogue prodrug, inhibits RNA-dependent RNA polymerase | ZEBOV, SUDV, and BDBV (in-vitro data only for BDBV)[79] | Rhesus macaques protected from lethal disease when remdesivir was used at 10 mg/kg dose for 12 days, initiated 3 days after ZEBOV challenge (100% survival, n=6); a significant reduction in plasma viral RNA compared to control was observed[79] | Phase 2–3 clinical trial (PALM trial) reported higher mortality at 28 days (200 mg loading dose on day 1, then 100 mg daily on days 2–13; 53·1% mortality) compared to ansuvimab (35·1%) and REGN-EB3 (33·5%);[75] phase 2 clinical trial (n=38; PREVAIL IV) reported a reduction in Ebola virus RNA in semen of Ebola survivors at 2–6 months in the remdesivir (100 mg per day for 5 days) treatment group[80] | 75,79–81 |
| Favipiravir | Nucleoside analogue, inhibits RNA polymerase and potential lethal mutagenic effect[82] | ZEBOV and SUDV (animal study only for SUDV)[83] | Partial protection of cynomolgus monkeys treated with favipiravir 2 days before infection with ZEBOV (60% survival in highest dose group—loading dose 250 mg/kg twice daily for 1 day, then 180 mg/kg twice daily for 12 days, n=5); drug concentration-dependent reduction in viral load observed[84] | Prospective, non-randomised clinical trial in Guinea (n=126) using favipiravir (6000 mg on day 1, then 2400 mg on days 2–10); participants with a high viral load (Ct <20) showed no decline in viral load with therapy and high mortality; no randomised control group was available to assess efficacy; no significant reduction in mortality compared to historical controls[85] | 82–85 |
| Ribavirin added to favipiravir | Ribavirin mechanism not fully understood but likely has multiple targets: targeting of inosine monophosphate dehydrogenase, leading to depletion of guanosine triphosphate pools; inhibition of viral translation initiation; blocking of RNA viral cap synthesis; inhibition of viral RNA polymerase; and viral mutagenesis[82] | ZEBOV | Ribavirin (5 or 10 mg/kg twice daily for 14 days) did not demonstrate benefit when added to favipiravir (180 mg/kg twice daily for 14 days), initiated 1–2 days before lethal ZEBOV challenge (survival rate 10% in the combination group *vs* 40% in the favipiravir monotherapy group, n=15 cynomolgus macaques), and did not lower the viral replication rate;[86] in cynomolgus macaques (n=4), ribavirin (30 mg/kg on days 1–3 then 15 mg/kg from day 4) reduced viral loads and delayed time to death by 2 days, but the survival rate was 0%[87] | .. | 82,86,87 |
| Galidesivir | Adenosine nucleoside analogue, inhibits viral RNA polymerase function | ZEBOV and SUDV (in-vitro data only for SUDV)[88] | Galidesivir (100 mg/kg twice daily as loading dose on day 1, then 25 mg/kg twice daily for 11 days) protected rhesus monkeys (n=6) against lethal ZEBOV challenge when administered 2 days after challenge (100% survival); four of six animals survived (67% survival) when administered 3 days after challenge[89] | Phase 1 study assessing pharmacokinetics and safety (n=126) in healthy participants; no clinically significant adverse events were reported and galidesivir was deemed to be safe and generally well tolerated[90] | 88–90 |

(Table 2 continues on next page)

| | Mechanism of action and target site | Reported *Ebolavirus* species targeted | Non-human primate studies | Clinical trials | Refs |
|---|---|---|---|---|---|
| (Continued from previous page) | | | | | |
| **Unlicensed and investigational mAb therapies for EVD** | | | | | |
| MBP-134 and MBP-431 (MBP-134 with extended half-life) | mAb cocktail of two broadly neutralising human mAbs, ADI-15878 (targeting the highly conserved conformational fusion-loop present in all Ebola viruses) and ADI-23774 (a specificity-matured mAb for SUDV glycoprotein binding affinity); recognises the broadly conserved base subdomain of the Ebola virus glycoprotein[32] | ZEBOV, SUDV, and BDBV (animal data);[32,91] and Taï Forest Ebola virus, Reston Ebola virus, and Bombali Ebola virus (in-vitro data only)[32] | MBP-134 (25 mg/kg single dose) protected rhesus macaques against ZEBOV (n=8) and SUDV (n=8) when administered 4–5 days after lethal challenge and cleared viraemia (100% survival);[91] MBP-134 also protected cynomolgus macaques against BDBV (n=6) when administered 7 days after lethal challenge and cleared viraemia (90% survival);[91] MBP-134, either 7·5 or 25 mg/kg single dose administered intravenously, or 15 mg/kg administered intramuscularly, protected rhesus macaques (n=18) from lethal disease 3–5 days after SUDV challenge (94% survival);[92] MBP-431 (5 or 15 mg/kg) administered intramuscularly 3 days after ZEBOV challenge protected rhesus macaques from lethal disease (100% survival, n=10)[92] | Planned clinical trial for use during recent SUDV outbreak in Uganda[93] | 32,91–93 |
| MBP-431 with or without remdesivir | See above | Combination evaluated only in SUDV | Improved survival in rhesus macaques (n=5 in each treatment group) challenged with SUDV; combination therapy with MBP-431 (15 mg/kg single dose) and remdesivir (10 mg/kg loading dose, followed by 5 mg/kg daily for 12 days) administered 6 days after lethal challenge reduced mortality (80% survival) compared to MBP-431 monotherapy (20%) or remdesivir monotherapy (20%)[94] | Planned clinical trial for use during recent SUDV outbreak in Uganda[93] | 93,94 |
| ZMapp | mAb cocktail comprising c13C6, which targets the glycan cap of the ZEBOV glycoprotein, and c2G4 and c4G7, which target the base region of the membrane-bound glycoprotein[95] | ZEBOV | ZMapp (50 mg/kg every 3 days for three doses) protected rhesus macaques (n=6) from lethal ZEBOV challenge (100% survival) when administered up to 5 days after challenge[96] | Phase 1–2 randomised, controlled trial (PREVAIL II; n=72) did not meet prespecified statistical threshold for efficacy (22% mortality in ZMapp group *vs* 37% in standard-of-care group);[97] phase 2–3 clinical trial (PALM trial; n=681) reported higher mortality at 28 days with ZMapp (50 mg/kg every 3 days for three doses; 49·7% mortality) compared with REGN-EB3 (33·5%) or ansuvimab (35·1%)[75] | 75,95–97 |

BDBV=Bundibugyo Ebola virus. EVD=Ebola virus disease. FDA=Food and Drug Administration. GP1=glycoprotein subunit 1. GP2=glycoprotein subunit 2. mAb=monoclonal antibody. SUDV=Sudan Ebola virus. ZEBOV=Zaire Ebola virus.

***Table 2:*** **Ebola antiviral therapies that have progressed to non-human primate studies and clinical trials**

PEP was 1 day. None of the individuals developed EVD, and all were negative for Ebola virus on PCR at day 14. Neither ansuvimab nor REGN-EB3 can be coadministered with rVSV-ZEBOV vaccine due to their impact on the replication of the rVSV-ZEBOV vector. Neither therapy has been evaluated for use in non-ZEBOV species.

## Post-exposure antivirals

Favipiravir (T-705) is a viral RNA polymerase inhibitor that has demonstrated efficacy in treating EVD in animal studies.[84,99] Favipiravir has demonstrated broad antiviral activity by targeting the catalytic domain of RNA-dependent RNA polymerase, which is conserved across many RNA viruses.[100] It has been approved for use in Japan for novel influenza infection. Favipiravir was used in the published case series by Jacobs and colleagues as PEP, given to four individuals assessed as being at intermediate or higher risk for developing EVD following occupational exposure to ZEBOV.[22] It was given in combination with mAb for the two highest risk cases. In this small case series, no individual developed EVD. Favipiravir has also been evaluated in a non-randomised clinical trial for treatment of EVD caused by ZEBOV in 126 individuals in Guinea.[85] In the group with a high viral load (Ct <20), favipiravir did not reduce viral load, and mortality was higher compared to historical reference data. These negative findings might relate to the lower than expected concentrations of favipiravir observed in participants, which were below the defined target plasma drug concentration, possibly related to disease effects on drug pharmacokinetics and the non-linear pharmacokinetic profile of favipiravir.[101] For both of these studies, the lack of a control group precludes assessment of efficacy for use in treatment or PEP.

The antiviral remdesivir, also an RNA polymerase inhibitor, has demonstrated antiviral activity against ZEBOV in vitro and in rhesus macaques, with antiviral activity also observed in other *Ebolavirus* species including SUDV.[79] Remdesivir was evaluated as an investigational agent in the PALM clinical trial and was found to be inferior to ansuvimab and REGN-EB3 with respect to mortality.[75] For this reason, WHO has given a conditional recommendation against the use of remdesivir for EVD.[98] However, its efficacy has not been evaluated in clinical trials for use in non-ZEBOV species.

### Search strategy and selection criteria

References for this Review were selected through searches in PubMed for relevant articles published from database inception to May 31, 2023, with the search terms "Ebola OR Ebola virus disease" or "Sudan virus", combined with the terms "vaccination OR immunisation", "occupational", "laboratory acquired infection", "prophylaxis", "post-exposure prophylaxis", or "management OR treatment". Articles identified through these searches, and relevant references cited within these articles, were reviewed. Articles published in English were reviewed. Non-peer reviewed references include national or international guidelines from the US Centers for Disease Control and Prevention, the UK Health Security Agency, and WHO.

In addition, antiviral activity was demonstrated in a phase 2 randomised clinical trial wherein remdesivir was compared to placebo for reduction of ZEBOV RNA in semen of male survivors.[80] A clinical trial to evaluate the efficacy of remdesivir for SUDV was planned during the recent outbreak in Uganda.[93]

Ribavirin is an antiviral agent licensed for use in chronic hepatitis C infection and respiratory syncytial virus infection in infants and patients who are immunocompromised. Limited antiviral activity has been demonstrated against ZEBOV in vitro[102,103] and in animal studies.[87] Combination ribavirin and favipiravir was previously demonstrated to have synergistic activity in an animal arenavirus infection model.[104] However, when evaluated in a non-human primate model of EVD, no mortality benefit or impact on viral load was observed with combination therapy compared to favipiravir monotherapy following lethal challenge with ZEBOV.[86] In addition, the well recognised effect of ribavirin causing haemolytic anaemia was a prominent adverse effect in the combination therapy group.

### PEP for SUDV

There are currently no published reports of PEP for SUDV. During the recent SUDV outbreak in Uganda, remdesivir and the investigational mAb MBP-134 (MappBio) were planned for evaluation in clinical trials as monotherapy and combination therapy for EVD.[93,105] MBP-134 is an mAb cocktail of two broadly neutralising mAbs, ADI-15878 and ADI-23774, that have demonstrated pan-Ebola virus activity in animal studies.[32,91,92] MBP-134 has also been evaluated in a modified form to extend the half-life of the mAbs, as a product that has been designated MBP-431.[91] Combination therapy with remdesivir and MBP-431 demonstrated significant benefit in rhesus macaques infected with SUDV infection, with greater survival observed with combination therapy than with either the mAb or antiviral alone.[94] Investigational vaccines active against SUDV have not been evaluated for use in a PEP setting.

## Special populations

There are limited data on the safety and efficacy of licensed vaccines and antivirals in pregnancy and in immunosuppressed individuals. Pregnant women and individuals with significant immunodeficiency were excluded from the rVSV-ZEBOV vaccine trials. However, more than 80 women were inadvertently vaccinated in early pregnancy or became pregnant shortly after vaccination in a trial undertaken in Sierra Leone, with no observable adverse effects.[106] In the phase 2–3 clinical trial evaluating ansuvimab, REGN-EB3, and remdesivir, pregnant women were not excluded but comprised only 6% (n=17) of participants.[75] Favipiravir has demonstrated potential teratogenicity in animal studies and is contraindicated in pregnancy.[107] Remdesivir has been used in pregnant women with severe COVID-19, with no serious safety signals identified in pregnancy to date; monitoring of maternal and infant outcomes is ongoing.[108]

Antiviral and mAb therapy use in patients who are immunosuppressed is not contraindicated. However, safety of the rVSV-ZEBOV live vaccine in this population is unknown. Given the potential for severe adverse outcomes with EVD in individuals who are immunosuppressed or pregnant, health-care or laboratory staff should be fully informed of the limited data on pre-exposure prevention or PEP in the event of occupational exposure in this setting.

## Conclusion

Significant advances in vaccine and therapeutic development have seen improved outcomes for individuals with EVD. However, these therapies have predominantly targeted ZEBOV, and clinical data on efficacy against SUDV are lacking. Outcomes of clinical trials on SUDV-specific vaccines, mAbs, and antivirals are eagerly awaited. In addition, safety data in special populations, such as pregnant women and people with immunosuppression, are needed for all *Ebolavirus* species. Occupational exposure to SUDV in outbreak management might prompt clinicians to seek use of unlicensed therapies for PEP, as was seen for cases of ZEBOV occupational exposure during outbreaks before licensed vaccines or mAbs became available.[20,22,24] Such approaches should ensure ethical use of off-label therapies and equitable access to individuals at highest risk.

#### Contributors

MAM, CKL, and DAW conceptualised the Review. MAM conducted the literature search. MAM, CKL, and DAW drafted the manuscript, which was edited and critically revised by EW, CM, and JM. All authors reviewed the final manuscript before submission for publication.

#### Declaration of interests

We declare no competing interests.

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